Resolving Myelin and Axonal Properties within the Same Voxel in Presence of Crossing Fibers by Combining Inversion Recovery and Diffusion Acquisitions

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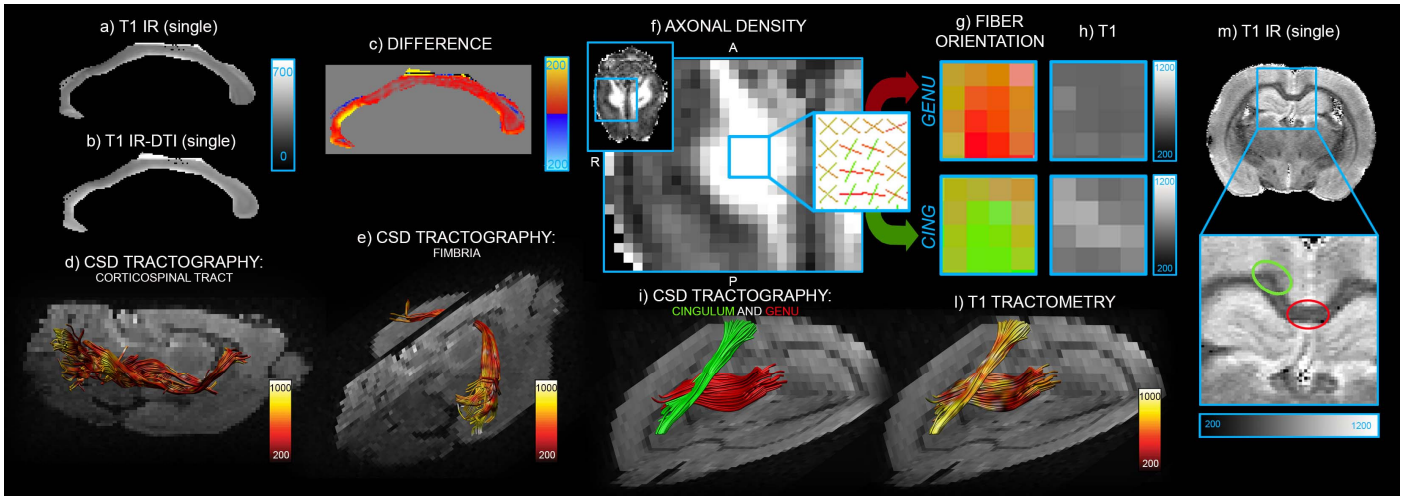
PURPOSE AND TARGET: White matter (WM) properties can be described by two distinct attributes: the axonal features (e.g., axonal diameter and density) and the myelination. MRI techniques have proven to be incredibly useful for characterizing WM over recent years: diffusion MRI and relaxometry allow, respectively, estimation of the diffusion tensor[1], reflecting largely axonal properties, and quantification of myelin content[2-3], both averaged over the image voxel. As more than 90% of WM voxels contain more than one fiber population[4], increasing specificity to distinct attributes of the WM depends fundamentally on disentangling the aforementioned quantitative metrics from the fibre *architectural paradigm.* While several methods have been proposed to measure the specific diffusion properties of each fiber population present within a single voxel[5], methods developed for assessing myelin to date provide only a single (average) myelin content of the voxel, irrespective of the architectural paradigm. This work addresses this limitation directly with a new acquisition & analysis strategy that combines inversion recovery (IR) with conventional diffusion tensor imaging (DTI)[6], and by acquiring CHARMED[5] data to calculate fiber orientations and volume fractions. For each fiber population within a voxel, we extract a specific longitudinal relaxation time T1 by exploiting the orientational dependence of the diffusion-weighted signal that has been previously inversion-prepared. As the relaxation time, T1, has been established as a good proxy for myelination[7], this method effectively succeeds, for the first time, in **resolving both axonal and myelin properties in presence of multiple fiber populations within a voxel**. This framework will be of interest to anyone interested in increasing specificity in MRI analysis of WM microstructure.

METHODS: To calibrate the inversion recovery (IR) prepared DTI (IR-DTI) sequence, both IR-DTI and conventional IR data were acquired on a human corpus callosum sample (single fiber population) with the following inversion times (TI): 60,100:25:500,550:50:700,800,900,1000,1250,1500,2000ms. An ex-vivo rat brain was scanned using the IR-DTI sequence with the following parameters: TI=200,325,450,500,650,1000ms, 30 gradient orientations, b=1000s/mm^2. A CHARMED protocol was also applied using 90 gradient orientations and max b=4000s/mm^2. Conventional high-resolution IR data were also acquired. CHARMED data were processed to obtain, for each voxel, two main orientations and two volume fractions (f1 and f2). The fitted CHARMED parameters were used to generate two diffusion tensors D1 and D2 for each voxel to input into the IR-DTI data analysis. The IR-DTI signal is fitted to $S/S_0=f1*(1-2*\exp(-TI/T1_1))*\exp(-b*D1)+f2*(1-2*\exp(-TI/T1_2))*\exp(-b*D2)$ in order to find $T1_1$ and $T1_2$. As such, two relaxation times, two main fiber orientations and two volume fractions are extracted for each voxel. The fitted orientations are also used to perform tractography using a CSD approach[8]. Due to the limited anatomical resolution of the scan, the cingulum bundle and the genu of the corpus callosum effectively cross within a voxel, providing a good test-bed for our approach.



RESULTS AND DISCUSSION: The T1 maps calculated on the human corpus callosum (a and b) show little differences (c) between conventional IR and the IR-DTI sequence, demonstrating the validity of the proposed sequence for single fiber configuration. The results on the ex-vivo rat brain demonstrate the ability of the method to resolve differential axonal and myelin properties for different fiber tracts, e.g., the corticospinal tract is characterised by a lower T1 (546 ms) than the fimbria, where T1=604 ms (d and e). The key result of this work is found in the area of overlap between the genu of the corpus callosum and the cingulum. CHARMED analysis (f and g) successfully recovers two distinct orientations in the crossing area (red and green) and the associated T1 maps (h) show different T1values for each fiber population. The tractometry analysis[9] (i and l) on the two bundles returns T1=757 ms for the genu and T1=843 ms for the cingulum. Similar differences are found measuring T1 separately in the two bundles (m) in the conventional IR maps at high resolution (where the fibers are spatially resolved). The results are consistent with the fact that the corpus callosum is more myelinated than the cingulum and myelin is inversely correlated with T1.

CONCLUSION: Our new method resolves both axonal and myelin properties in the presence of crossing fibers, obtaining tract-specific values of the axonal density and T1, that is considered a proxy for myelination.

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